

Claims:

- Sub C1
1. A composition for inducing chondrogenesis and/or skeletal development in a vertebrate, the composition comprising:
- (a) a RAR antagonist; and
 - (b) a pharmaceutically acceptable carrier.
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2. The composition as claimed in claim 1, further comprising a protein selected from the group consisting of a bone morphogenic protein (BMP), an osteogenic protein (OPS) and a cytokine and combinations thereof.
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3. The composition as claimed in claim 2, wherein said BMP is selected from the group consisting of BMP-2, BMP-4, and BMP-5.
- no 1.
4. The composition as claimed in claim 3, wherein said osteogenic protein is OP-
- Sub C2
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5. The composition of claim 1, wherein the RAR antagonist is present in an amount capable of stimulating chondrogenesis and associated differentiation of skeletal progenitor cells.
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6. The composition of claim 1, wherein said composition is provided as a solution, suspension, gel, matrix, film, paste, pill, tablet or encapsulated within liposomes.
- no
7. The composition of claim 1, wherein said composition is administered via intra-articular injection.
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- no
8. The composition of claim 1, wherein said composition is provided within a biodegradable implantable matrix.

1- Sub C3
9. The use of a composition comprising an RAR antagonist and a pharmaceutically acceptable carrier, for inducing chondrogenesis.

10. The use of a composition of claim 9 wherein said use is *in vitro*.

11. The use of a composition of claim 9 wherein said use is *in vivo*.

12. A morphogenic device for implantation in a vertebrate, the device comprising:

- 10 no
(a) an implantable biocompatible carrier; and
(b) an RAR antagonist dispersed within or on said carrier.

no 13. The device according to claim 12, wherein said carrier comprises demineralized, protein-extracted, particulate, allogenic or xenogenic bone.

15 no 14. The device according to claim 12, wherein said device comprises mineral-free, delipidated Type I insoluble collagen.

no 15. The device according to claim 12, wherein said device comprises a biodegradable sponge.

20 Sub C1
16. A method for producing a chondrocyte from a chondroprogenitor mesenchymal cell comprising contacting said chondroprogenitor mesenchymal cell with an RAR antagonist agent *in vitro*.

Sub C4
25 17. A method for promoting *in vivo* integration of an implantable prosthetic device, into a target cartilage tissue of a vertebrate, the method comprising the steps of:

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(a) providing on a surface of the prosthetic device a composition comprising an RAR antagonist and a pharmaceutically acceptable carrier and
(b) implanting the device in a vertebrate, at a site where the target cartilage tissue and surface of the prosthetic device are maintained at least partially in contact

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for a time sufficient to permit enhanced tissue growth between the target cartilage tissue and the device.

18 The method according to claim 19, wherein said target tissue is bone.

19. A method of treating a cartilage associated degenerative condition in a vertebrate comprising the step of administering a pharmaceutical composition as claimed in claim 1.

20. A method for promoting chondrogenesis and associated bone tissue formation at a site of skeletal surgery in a vertebrate, the method comprising the steps of delivering an RAR antagonist composition at the site of skeletal surgery wherein such delivery promotes the formation of new bone tissue.

21. A method for repairing large segmental skeletal gaps and non-union fractures arising from trauma or surgery in vertebrates, the method comprising delivering a RAR antagonist composition at the site of the segmental skeletal gap or non-union fracture wherein such delivery promotes chondrogenesis which mediates the formation of new bone tissue.

22. A method for aiding the attachment of implantable prosthesis at cartilaginous sites and for maintaining the long term stability of the prostheses in vertebrates, the method comprising coating selected regions of an implantable prosthesis with a RAR antagonist composition and implanting the coated prosthesis into a cartilaginous site wherein such implantation promotes the formation of new cartilage tissue.

23 A method of producing cartilage at a cartilage defect *in vivo*, said method comprising:
- implanting into the defect a population of chondrogenic cells which have been cultured in the presence of a RAR antagonist

Sub
C5

24. A method for treating degenerative joint disease characterized by cartilage degeneration, said method comprising:

- delivering a therapeutically effective amount of an RAR antagonist to the site of disease.

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no 25. The method according to claim 24, wherein said RAR antagonist is delivered by intra-articular injection.

no 26. The method according to claim 24, wherein said disease is arthritis.

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27. An implantable prosthetic device for repairing an orthopedic defect, injury or anomaly in a vertebrate, said device comprising:

(a) a prosthetic implant having a surface region implantable adjacent or within a target tissue;

15 (b) an RAR antagonist composition disposed on said surface region in an amount sufficient to promote enhanced chondrogenesis and associated bone tissue growth into the surface.

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28. The use of a composition comprising an RAR antagonist for inhibiting RAR
20 activity and stimulating chondroblast differentiation.

29. The use of an RAR antagonist for decreasing transcriptional activation of the RA receptor and stimulating chondroblast differentiation.

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